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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/931,285	STUELPNAGEL ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *12/2001* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

1. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

2. The disclosure is objected to because of the following informality: some of references recited in the specification are incomplete. For example, in page 2, line 14, the specification recites "[C]ordor et al., Science 261(1993)" . In page 10, line 4, the specification recites "[J]enkins et al., Chem. Soc. Rev. (1995) pp169-176". However, applicant does not provide volume for these references. For example, in page 16, lines 3-5, the specification recites "[A]n extensive guide to the hybridization of nucleic acids is found in Tijssen, Techniques in Biochemistry and Molecular Biology-Hybridization with Nucleic Acid Probes, 'overview of principles of hybridization and the strategy of nucleic acid assays'(1993).". However, applicant does not provide volume and page numbers for this reference.

Appropriate correction is required.

Claim Objections

3. Claim 1 is objected to because of the following informalities: (1) "target nucleic acid" in line 2 of step a) should be "a target nucleic acid"; and (2) "said first primers ro said target nucleic acid" should be "said first primers or said target nucleic acid" since the word "or" is misspelled.

4. Claims 1, 2, 12, 13, and 16 are objected to because of the following informalities: no period should appear after the label of each step, e.g., "a." should be --a)--.

5. Claim 12 are objected to because of the following informality: "target nucleic acid" in line 2 of step a) should be "a target nucleic acid".

6. Claim 16 is objected to because of the following informality: "target nucleic acid" in lines 1 and 2 should be "a target nucleic acid".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 is rejected as vague and indefinite in view of the phrase "said target nucleic acid flanking a first target sequence" in step b) and the phrase "said target nucleic acid flanking a second target sequence" in step c) since it is unclear whether a first target sequence or a second

target sequence is part of said target nucleic acid or not. According to the meaning of "flanking", it appears that a first target sequence or a second target sequence is on the side of said target nucleic acid and is different from said target nucleic acid. However, from the steps (d) and (g), it appears that said target nucleic acid comprises a first target sequence and a second target sequence. Please clarify.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 1-3, 8-12, 16, and 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Chee *et al.,* (US Patent No. 6,355,431 B1, filed on March 2000, priority date: April 20, 1999).

The applied reference has a common inventor, Mark S. Chee, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35

U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The rejection is based on that an enzyme recited in step b) of independent claims 1 and 16 is a ligase.

Chee *et al.*, teach detection of nucleic acid amplification reactions using bead arrays. As shown in Figures 7A, 7B, 7C, 7D, 7E and 7F, an immobilized first OLA primer 45 was hybridized with a target sequence 25 and a second OLA primer 50. Following the addition of ligase, the first and second OLA primers were ligated to form a ligated oligonucleotide 56. Following denaturation to remove the target nucleic acid, the immobilized ligated oligonucleotide was distributed on an array. An RCA probe 57 and polymerase were added to the array resulting in amplification of the circular RCA probe 58 (see column 6, last paragraph and column 7, lines 1 and 2).

Regarding claims 1-3, since the first OLA primer 45 immobilized on a bead is hybridized with a target sequence 25 (see column 6, last paragraph), Chee *et al.*, provide a composition comprising first primers and a target nucleic acid wherein either said first primers or said target nucleic acid is immobilized to at least one solid support and teach i) of step b) of claim 1. Since Chee *et al.*, teach that unligated olignucleotides are removed by washing under appropriate stringency conditions (see column 18, last paragraph) and claim 1 does not require that ii) of step b) must happened before iii) of step b), ii) of step b) of claim 1 is anticipated by Chee *et al.*. Since, Chee *et al.*, teach that, following the addition of ligase, the first and second OLA primers

are ligated to form a ligated oligonucleotide 56 and said target nucleic acid is not consumed (see column 6, last paragraph and Figures 7B and 7C), iii) of step b) of claim 1 is anticipated by Chee *et al.*, wherein the ligase and oligonucleotide 56 are an enzyme and first modified primers respectively as recited in iii) of step b) of claim 1. Since Chee *et al.*, teach to repeat steps a) and b) of claim 1 of this instant application (see column 59, claims 1 and 2) and claim 2 does not require that second primers are different from first primers and second modified primers are different from first modified primers, step c) of claim 1 and claim 2 are anticipated by Chee *et al.*, wherein repeating steps a) and b) of claim 1 of this instant application is considered as performing a second analysis of said target nucleic acid as recited in step c) of claim 1 and claim 2. Since Chee *et al.*, teach to contact said modified first primer nucleic acids with an array comprising nucleic acids and detect the presence of the modified primer nucleic acids and claim 3 does not require that second modified primers are different from first modified primers, claim 3 is anticipated by Chee *et al.*.

Regarding claims 8-10, since Chee *et al.*, indicates that target nucleic acid can be human genomic DNA (see column 7, lines 41-57 and column 9, lines 14-20), claims 8-10 are anticipated by Chee *et al.*, wherein an organism recited in claims 9 and 10 is human.

Regarding claim 11, since Figures 2B and 3B shows that the ligation chain reaction can be performed in the presence of a primer comprising an adapter sequence (see Figures 2B and 3B, and column 6, lines 9-23), Chee *et al.*, teach that at least one of said first and second primers comprising an adapter sequence as recited in claim 11.

Regarding claim 12, since the first OLA primer 45 immobilized on a bead is hybridized with a target sequence 25 (see column 6, last paragraph), Chee *et al.*, provide a composition

comprising first primers and a target nucleic acid as recited in step a) and teach step b) wherein a hybridized complex formed by the first OLA primer 45 and a target sequence 25 is a first ligation complex as recited in step b). Since Chee *et al.*, teach that unligated oligonucleotides are removed by washing under appropriate stringency conditions (see column 18, last paragraph) and claim 12 does not require that step c) must happened before step b), step c) of claim 12 is anticipated by Chee *et al.*. Since, Chee *et al.*, teach that, following the addition of ligase, the first and second OLA primers are ligated to form a ligated oligonucleotide 56 (see column 6, last paragraph and Figures 7B and 7C), step d) of claim 12 is anticipated by Chee *et al.*, wherein the ligase and oligonucleotide 56 are a ligation enzyme and a first ligation product respectively as recited in step d). Since Chee *et al.*, teach that the ligated oligonucleotides are eluted from the target nucleic acid using denaturing conditions (see column 18, last paragraph), Chee *et al.*, teach step e) of the claim. Since Chee *et al.*, teach to repeat steps a) to f) of claim 1 (see column 59, claims 1 and 2) and steps f) and g) of the claim is anticipated by Chee *et al.*.

Regarding claims 16 and 20, since the first OLA primer 45 immobilized on a bead is hybridized with a target sequence 25 (see column 6, last paragraph), Chee *et al.*, provide a composition comprising first primers and a target nucleic acid wherein said first primers is immobilized to at least one solid support as recited in step a) of claim 16 and claim 20 and teach i) of step b) of claim 16. Since Chee *et al.*, teach that unligated oligonucleotides are removed by washing under appropriate stringency conditions (see column 18, last paragraph) and claim 16 does not require that ii) of step b) must happened before iii) of step b), ii) of step b) of claim 16 is anticipated by Chee *et al.*. Since, Chee *et al.*, teach that, following the addition of ligase, the first and second OLA primers are ligated to form a ligated oligonucleotide 56 and said

target nucleic acid is not consumed (see column 6, last paragraph and Figures 7B and 7C), iii) of step b) of claim 16 is anticipated by Chee *et al.*, wherein the ligase and oligonucleotide 56 are an enzyme and first modified primers respectively as recited in iii) of step b) of claim 16. Since Chee *et al.*, teach to repeat steps a) and b) of claim 16 (see column 59, claims 1 and 2), said first nucleic acid taught by Chee *et al.*, is reused as recited in step c) of claim 16.

Regarding claim 18, since Chee *et al.*, indicates that target nucleic acid can be human genomic DNA (see column 7, lines 41-57 and column 9, lines 14-20), claim 18 is anticipated by Chee *et al.*.

Regarding claim 19, since Chee *et al.*, indicates that target nucleic acid can be immobilized on a solid-phrase surface (see column 18, last paragraph), claim 19 is anticipated by Chee *et al.*.

Therefore, Chee *et al.*, teach all limitations recited in claims 1-3, 8-12, 16, and 18-20.

11. Claims 1, 2, 4-10, 12, 13, 15, 16, and 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Chee *et al.*, (April 20, 1999).

The applied reference has a common inventor, Mark S. Chee, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The rejection is based on that an enzyme recited in step b) of independent claims 1 and 16 is an enzyme to extend said first primer to form a first newly synthesized strand (see below).

Chee *et al.*, teach a method for detecting a target nucleic acid sequence comprising: a) hybridizing a first primer to a first target sequence to form a first hybridization complex; b) contacting said first hybridization complex with a first enzyme to extend said first primer to form a first newly synthesized strand and form a nucleic acid hybrid that comprises an RNA polymerase promoter; c) contacting said hybrid with a RNA polymerase that recognizes said RNA polymerase promoter and generates at least one newly synthesized RNA strand; d) contacting said newly synthesized RNA strand with an array comprising: i) a substrate with a surface comprising discrete sites; and ii) a population of microspheres comprising at least a first subpopulation comprising a first capture probe; such that said first capture probe and the modified primer form an assay complex; wherein said microspheres are randomly distributed on said surface; and e) detecting the presence of the newly synthesized RNA strand. Steps a) through c) of above method for detecting a target nucleic acid sequence are repeated prior to step d) (see column 61, claims 14 and 15).

Regarding claims 1, 2, and 16, since Chee *et al.*, teach to hybridize a first primer to a first target sequence to form a first hybridization complex wherein the first target sequence is immobilized on a solid-phase surface (see column 18, last paragraph and claim 14 in column 61), Chee *et al.*, provide a composition comprising first primers and a target nucleic acid wherein said target nucleic acid is immobilized to at least one solid support as recited in step a) of claims 1 and 16 and teach i) of step b) of claims 1 and 16. Since Chee *et al.*, teach to contact said first hybridization complex with a first enzyme to extend said first primer to form a first newly

synthesized strand and form a nucleic acid hybrid that comprises an RNA polymerase promoter and the process does not consume said target nucleic acid, Chee *et al.*, teach iii) of step b) of claims 1 and 16 wherein an enzyme and first modified primers as recited in iii) of step b) of claims 1 and 16 are a first enzyme to extend said first primer to form a first newly synthesized strand and a first newly synthesized strand. Since Chee *et al.*, teach to remove the unextended or unreacted primers from the assay mixture (see column 32, lines 20-31), ii) of step b) of claims 1 and 16 is anticipated by Chee *et al.*. Since Chee *et al.*, teach that steps a) through c) of the method for detecting a target nucleic acid sequence are repeated prior to step d) (see column 61, claims 14 and 15) and claim 2 does not require that second primers are different from first primers and second modified primers are different from first modified primers, step c) of claims 1 and 16, and claim 2 are anticipated by Chee *et al.*, wherein steps a) through c) of the method for detecting a target nucleic acid sequence taught by Chee *et al.*, is considered as performing a second analysis of said target nucleic acid as recited in step c) of claims 1 and 16 and claim 2.

Regarding claims 4-7, since Chee *et al.*, teach to contact said hybrid with a RNA polymerase that recognizes said RNA polymerase promoter and generates at least one newly synthesized RNA strand (see column 61, claim 14), claim 2 does not require that second modified primers are different from first modified primers, claim 4 is anticipated by Chee *et al.*, wherein newly synthesized RNA strands are first and second amplicons. Since Chee *et al.*, teach to contact a newly synthesized RNA strand with an array comprising nucleic acids and detect the presence of the newly synthesized RNA strand (see column 61, claim 14), Chee *et al.*, teach to detect said first and second amplicons as recited in claim 5. Since Chee *et al.*, teach that the

label can be incorporated into a newly synthesized nucleic acid strand during the process of the synthesis (see column 30, lines 35-56), claims 6 and 7 are anticipated by Chee *et al.*.

Regarding claims 8-10 and 18, since Chee *et al.*, indicates that target nucleic acid can be human genomic DNA (see column 7, lines 41-57 and column 9, lines 14-20), claims 8-10 and 18 are anticipated by Chee *et al.*, wherein an organism recited in claims 9 and 10 is human.

Regarding claims 12, 13, and 15, since Chee *et al.*, teach to hybridize a first primer to a first target sequence to form a first hybridization complex wherein the first target sequence is immobilized on a solid-phase surface (see column 18, last paragraph and claim 14 in column 61), Chee *et al.*, provide a composition comprising first primers and a target nucleic acid as recited in step a) of claim 12 and teach step b) of claims 1 and 16. Since Chee *et al.*, teach to contact said first hybridization complex with a first enzyme to extend said first primer to form a first newly synthesized strand and form a nucleic acid hybrid that comprises an RNA polymerase promoter, Chee *et al.*, teach step d) of claim wherein a first enzyme to extend aid first primer to form a first newly synthesized strand taught by Chee *et al.*, is considered to be a ligation enzyme recited in step d) of claim 12 since this enzyme extends said first primer to form a first newly synthesized strand. Since Chee *et al.*, teach to remove the unextended or unreacted primers from the assay mixture (see column 32, lines 20-31), step c) of claim 12 is anticipated by Chee *et al.*. Since Chee *et al.*, teach to remove the target nucleic acid after the ligation reaction, step e) of claim 12 is anticipated by Chee *et al.*. Since Chee *et al.*, teach that steps a) through c) of the method for detecting a target nucleic acid sequence are repeated prior to step d) (see column 61, claims 14 and 15) and detection of a newly synthesized RNA strand, and claim 12 does not require that second ligation primers are different from first ligation primers and second ligation products are

different from first ligation products, steps f) and g) of claim 2 and claims 13 and 15 are anticipated by Chee *et al.*, wherein synthesis of a RNA strand in the presence of a RNA polymerase taught by Chee *et al.*, is considered as the amplification reaction recited in claims 13 and 15.

Regarding claim 19, since Chee *et al.*, indicates that target nucleic acid can be immobilized on a solid-phrase surface (see column 18, last paragraph), claim 19 is anticipated by Chee *et al.*.

Regarding claim 20, since Chee *et al.*, indicates that primers can be immobilized on a solid-phrase surface (see Figure 7A), claim 20 is anticipated by Chee *et al.*.

Chee *et al.*, teach all limitations recited in claims 1, 2, 4-10, 12, 13, 15, 16, and 18-20.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claim 17 is rejected under 35 U.S.C. 103(a) as being obvious over Chee *et al.*, (April 20, 1999).

The applied reference has a common inventor, Mark S. Chee, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of Chee *et al.*, have been summarized previously, *supra.* Since Chee *et al.*, teach to repeat steps a) through c) in a method for detecting a target nucleic acid sequence (see

column 59, claim 2 and column 61, claim 15), Chee *et al.*, disclose to reuse said target nucleic acid at least once.

Chee *et al.*, do not disclose to reuse said target nucleic acid at least five times as recited in claim 17.

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 16 using said target nucleic acid recited in claim 16 at least five times in view of the patents of Chee *et al.*. One having ordinary skill in the art would have been motivated to do so because Chee *et al.*, have successfully used said target nucleic acid recited in claim 16 twice and reusing the same target nucleic acid at least five times would cause more first modified primers recited in claim 16 to be made. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to reuse said target nucleic acid recited in claim 16 at least five times.

14. Claims 21-23 are rejected under 35 U.S.C. 103(a) as being obvious over Chee *et al.*, (April 20, 1999).

The applied reference has a common inventor, Mark S. Chee, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which

corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of Chee *et al.*, have been summarized previously, *supra.* Chee *et al.*, disclose to two target nucleic acids, a first and second target nucleic acids wherein the first and the second target nucleic acids are substantially complementary each other (see column 59, claims 3). The method for detecting a first target nucleic acid sequence taught by Chee *et al.*, (see column 59, claim1) is considered as a single reaction.

Chee *et al.*, do not disclose to use 10-100 different target nucleic acids in a single reaction as recited in claims 21-23.

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have performed the method recited in claim 16 using 10-100 different target nucleic acids in a single reaction in view of the patents of Chee *et al.*. One having ordinary skill in the art would have been motivated to do so because Chee *et al.*, have successfully used two different target nucleic acids in the method recited in claim 16 and using 10-100 different target nucleic acids in the method recited in claim 16 would enhance to make

different modified primers. One having ordinary skill in the art at the time the invention was made would have been a reasonable expectation of success to make different modified primers using the method recited in claim 16.

15. Claim 14 is rejected under 35 U.S.C. 103(a) as being obvious over Chee *et al.*, (April 20, 1999) in view of Barany *et al.*, (US Patent No. 6,027,889, filed on May 28, 1997, priority date: May 29, 1996).

The applied reference has a common inventor, Mark S. Chee, with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). For applications filed on or after November 29, 1999, this rejection might also be overcome by showing that the subject matter of the reference and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person. See MPEP § 706.02(l)(1) and § 706.02(l)(2).

The teachings of Chee *et al.*, have been summarized previously, *supra.*

Chee *et al.*, do not disclose to amplify said first and second ligation products in the presence of DNA polymerase and dNTPs as recited in claim 14.

Barany *et al.*, teach to amplify a ligation product in the presence of DNA polymerase and dNTPs and detect the amplified product (see Figure 10, Examples 4-6 in columns 41-46 and claim 1 in columns 80-82).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have amplified said first and second ligation products in the presence of DNA polymerase and dNTPs and detected the first and second amplicons as recited in claims 13 and 14 in view of the patents of Chee *et al.*, and Barany *et al.*. One having ordinary skill in the art would have been motivated to do so because Barany *et al.*, have successfully amplified a ligation product in the presence of DNA polymerase and dNTPs and have successfully detected the amplified product, and the simple replacement of one polymerase with known properties (i.e., a RNA polymerase) from another polymerase with known properties (i.e.,a DNA polymerase) during the process of amplifying the ligation product would have been, in the absence of convincing evidence to the contrary, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made because the replacement would not change the method steps of claim 16.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1-5, 8, 9, 12, 13, 15, 16, and 18-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No.6,355,431 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims in this instant application is either anticipated by, or would have been obvious over, the reference claims. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

Regarding claims 1, 2, and 16, since claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach to hybridize a first primer to a first target sequence to form a first hybridization complex and breadth of claims 14 and 15 of U.S. Patent No.6,355,431 B1 covers either a target nucleic acid immobilized on a solid-phase surface or a target nucleic acid in a solution, claims 14 and 15 of U.S. Patent No.6,355,431 B1 provide a composition comprising first primers and a target nucleic acid wherein said target nucleic acid is immobilized to at least one solid support as recited in step a) of claims 1 and 16 and teach i) of step b) of claims 1 and 16. Since claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach to contact said first hybridization complex with a first enzyme to extend said first primer to form a first newly synthesized strand and form a nucleic acid hybrid that comprises an RNA polymerase promoter and the process does not consume said target nucleic acid, Chee *et al.*, teach iii) of step b) of claims 1 and 16 wherein an enzyme and first modified primers as recited in iii) of step b) of claims 1 and 16 are a first enzyme to extend said first primer to form a first newly synthesized strand and a first newly synthesized strand. Although claims 14 and 15 of U.S. Patent No.6,355,431 B1 do not teach to remove unhybridized first primers as recited in ii) of step b) of claims 1 and 16, it would be *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to remove unhybridized first primers in order to reduce the interference from unhybridized first primers when he or she perform iii) of step b) of claims 1 and 16. Since U.S. Patent No.6,355,431 B1 teach that steps a) through c) of the method for detecting a target nucleic acid sequence are repeated prior to step d) and claim 2 does not require that second primers are different from first primers and second modified primers are different from first modified primers, step c) of claims 1 and 16, and claim 2 are anticipated by claims 14 and 15 of U.S.

Patent No.6,355,431 B1 wherein repeating steps a) through c) taught by claims 14 and 15 of U.S. Patent No.6,355,431 B1 is considered as performing a second analysis of said target nucleic acid as recited in step c) of claims 1 and 16 and claim 2.

Regarding claims 4 and 5, since claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach to contact said hybrid with a RNA polymerase that recognizes said RNA polymerase promoter and generates at least one newly synthesized RNA strand, claim 2 does not require that second modified primers are different from first modified primers, claim 4 is anticipated by claims 14 and 15 of U.S. Patent No.6,355,431 B1 wherein newly synthesized RNA strands are first and second amplicons. Since claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach to contact a newly synthesized RNA strand with an array comprising nucleic acids and detect the presence of the newly synthesized RNA strand, claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach to detect said first and second amplicons as recited in claim 5.

Regarding claims 8, 9, and 18, since breadth of claims 14 and 15 of U.S. Patent No.6,355,431 B1 covers a target nucleic acid from any source such as a genomic DNA from an organism, claims 8, 9, and 18 are anticipated by claims 14 and 15 of U.S. Patent No.6,355,431 B1.

Regarding claims 12, 13, and 15, since claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach to hybridize a first primer to a first target sequence to form a first hybridization complex and breadth of claims 14 and 15 of U.S. Patent No.6,355,431 B1 covers either a target nucleic acid immobilized on a solid-phase surface or a target nucleic acid in a solution, claims 14 and 15 of U.S. Patent No.6,355,431 B1 provide a composition comprising first primers and a target nucleic acid as recited in step a) of claim 12 and teach step b) of claim 12. Since claims 14 and

15 of U.S. Patent No.6,355,431 B1 teach to contact said first hybridization complex with a first enzyme to extend said first primer to form a first newly synthesized strand and form a nucleic acid hybrid that comprises an RNA polymerase promoter, claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach step d) of claim 12 wherein a first enzyme to extend said first primer to form a first newly synthesized strand taught by claims 14 and 15 of U.S. Patent No.6,355,431 B1 is considered to be a ligation enzyme recited in step d) of claim 12 since this enzyme extends said first primer to form a first newly synthesized strand. Although claims 14 and 15 of U.S. Patent No.6,355,431 B1 do not teach to remove unhybridized first primers as recited in ii) of steps c) and e) of claim 12, it would be *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to remove unhybridized first primers in order to reduce the interference from unhybridized first primers when he or she perform steps c) and e) of claim 2. Since claims 14 and 15 of U.S. Patent No.6,355,431 B1 teach that steps a) through c) of the method for detecting a target nucleic acid sequence are repeated prior to step d) and detection of a newly synthesized RNA strand, and claim 12 does not require that second ligation primers are different from first ligation primers and second ligation products are different from first ligation products, steps f) and g) of claim 12 and claims 13 and 15 are anticipated by claims 14 and 15 of U.S. Patent No.6,355,431 B1 wherein synthesis of a RNA strand in the presence of a RNA polymerase taught by claims 14 and 15 of U.S. Patent No.6,355,431 B1 is considered as the amplification reaction recited in claims 13 and 15.

Regarding claims 19 and 20, since breadth of claims 14 and 15 of U.S. Patent No.6,355,431 B1 covers either a target nucleic acid immobilized on a solid-phase surface or a

target nucleic acid in a solution and covers either first primers immobilized on a solid-phase surface or first primers in a solution, claims 19 and 20 is anticipated by claims 14 and 15 of U.S. Patent No.6,355,431 B1.

Regarding claim 3, since claims 1, 2, and 6 of U.S. Patent No.6,355,431 B1 teach to detect the presence of the modified primer nucleic acid and claim 3 does not require that the first and second modified primers are different, claims 1 and 2 of U.S. Patent No.6,355,431 B1 teach claim 3.

Therefore, although claims 1-5, 8, 9, 12, 13, 15, 16, and 18-20 in this instant application are not identical to claims 1-20 of U.S. Patent No. 6,355,431 B1, claims 1-20 of U.S. Patent No. 6,355,431 B1 are directed to the same subject matter and fall entirely within the scope of claims 1-5, 8, 9, 12, 13, 15, 16, and 18-20 in this instant application. In other words, claims 1-5, 8, 9, 12, 13, 15, 16, and 18-20 in this instant application are anticipated by claims 1-20 of U.S. Patent No.6,232,075B1.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank W Lu whose telephone number is 703-305-1270. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on 703-308-1152. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Frank Lu
PSA
October 9, 2003